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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,192	08/09/2001	Dan W. Denney JR.	GENITOPE-06493	5113

7590 07/12/2006

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,192	DENNEY, DAN W.	
	Examiner	Art Unit	
	Christopher H. Yaen	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: Denney D.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/26/2006 has been entered.

2. Claim 1-34 are canceled without prejudice or disclaimer.

3. Claims 35-39 are pending and examined on the merits.

NEW REJECTIONS

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 35-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cleary et al (Cell, 1986, Vol. 44, pp. 97-106) in view of Levy et al (Journal of

Experimental Medicine, 1988, Vol. 168, pp. 475-489) and Embleton et al (Nucleic Acids Research, 1992, Vol. 20, pp. 3831-3837).

a. Cleary et al teach instance of patients whose B cell tumors escaped the therapeutic effects of a monoclonal anti-idiotype antibody because of the emergence of subclones that showed changes in their Ig idiotopes (page 97, second column, lines 36-39) Cleary et al suggest that the idiotype heterogeneity unmasked by the anti-idiotype therapy resulted from somatic mutations within the variable region because the variant subclones were derived from the same original clone of neoplastic B-cells, and the same patterns of bands for rearranged Ig genes were detected (page 97, second column, lines 40-47). To confirm this hypothesis, Cleary et al cloned and sequences the functional heavy chain Ig genes from multiple independent isolates of a patients tumor cell population to conclude that point mutations in the variable regions accounted for the loss of idiotype following antibody therapy (page 97, second column, lines 48-54 and page 103, first column, lines 1-6 under the heading "Discussion"). Cleary et al also teach a marked heterogeneity in the variable region sequences of the tumor cell population prior to anti-idiotype therapy, having significant clustering of amino acid substitutions in CDR2 (page 97, second column, line 54 to page 98, first column, line 3 and page 103, second column, lines 26-28). Cleary et al teach that the clustering of mutation in the CDR2 after anti-idiotype therapy can be attributed in part to the strong negative selection exerted by the 7D11 antibody (page 104, first column, first paragraph). Cleary et al do not teach a

multivalent idiotypic vaccine which would comprise the variant Vh sequences which would comprise more than one idiotype and variant Vl sequence which would comprise more than one idiotype.

b. Levy et al corroborates the teaching of Cleary et al regarding the Vh sequences from multiple isolated of human B cell lymphoma (page 475, lines 19-23) and further teach that the light chain genes of human lymphoma cells mutate independently from heavy chain genes (page 476, lines 7-13).

c. Embleton et al teach in-cell PCR allowing for the linking and amplification of the expressed Vh and Vl within a single B-lymphocyte in order to preserve the particular combination of Vh and Vl within a lymphocyte (page 3831, second column, lines 17-18). Embleton et al teach that this method is superior to the prior art methods of PCR cloning of Ig regions which lost the natural combination of the heavy and light chains and required artificial recombination which had the potential to be dominated by promiscuous chains leading to different affinities and specificities (page 3831, second column, lines 8-16).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make a multivalent composition for idiotypic vaccination of a patient having a B-cell lymphoma by amplify and link the Vh and Vl chains of a multitude of B-lymphoma cells and recombinatly expressing the recombinant variable chains while retaining the original combinations of heavy and light chains in host cells. One of skill in the art would have been motivated to do so by the teachings of Cleary et al on the emergence of malignant B-cells which escaped anti-idiotype therapy due to

somatic mutations with the variable regions and the evidence presented by Cleary regarding the existence of heavy chain heterogeneity before the anti-idiotype therapy; the teachings of Levy et al on the presence of heterogeneity in the light chain of human B-cell lymphomas, and the teachings of Embleton regarding improvements in the PCR cloning of immunoglobulin genes from B-lymphocytes which preserves the natural paring of heavy chain and light chain and avoids the problems associated with the screening of artificial combinations. One of skill in the art would have been motivated to include a multitude of natural combinations of Vh and Vl sequences from the patients B-cell lymphomas in order to insure that an immune response could be raised to more than just one population of B-cells having a specific combination of Vh and Vl sequences because although it is evidence that a single clonal event precipitated the B-cell lymphoma, somatic mutations accumulate within both the heavy and light chains of the lymphoma.

Therefore, the claims of the instant invention are deemed obvious as a whole over the prior art cited.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher Yaen
Art Unit 1643
July 7, 2006

CHRISTOPHER H. YAEN
PRIMARY EXAMINER